

**Amendments to the Specification:**

Please replace paragraph beginning on page 8, line 4, with the following amended paragraph:

--Figure 1 shows two mechanisms for Interaction-dependent Enzyme Activation (IdEA). Figure 1A. Ligand-dependent circular permutations of an enzyme are formed by linking the native termini ~~into an “ $\alpha-\omega$ ” domain~~, and severing the polypeptide chain in a ~~solvent exposed loop~~ the “ $\mu$ ” domain to generate new carboxy and amino termini~~μ1 and μ2 subdomains~~. The circularly permuted enzyme can~~μ1 and μ2~~ refold to form an active enzyme when and only when the new termini ~~they~~ are brought together by an interaction of interaction of heterologous domains fused to the new their termini. The interaction can be direct or mediated by a second molecule (the ligand). The ligand-binding domains can include but are not limited to single-chain antibody fragments (scFv) and constrained peptides scaffolded on a carrier protein (csp). Versatile hydrolytic enzymes such as  $\beta$ -lactamases can be used to confer multiple selectable phenotypes including antibiotic resistance, color, death (prodrug, for inhibitor screens), and auxotrophic growth. Figure 1B. Interaction-dependent fragment complementation requires enzyme  $\alpha$  and  $\omega$  fragments which can reform to form active enzyme when and only when they are brought together by an interaction of heterologous domains fused to their termini.--